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Reprinted from the
Transactions of the Royal Society
of Tropical Medicine and Hygiene.
Vol. XXXII. No. 1 pp. 67-92
(*Issued 25th June, 1938*)

EARLY DISCOVERIES REGARDING THE PARASITE OF ORIENTAL SORE.

(With an English Translation of the Memoir by P. F. Borovsky: "On Sart Sore." 1898.)

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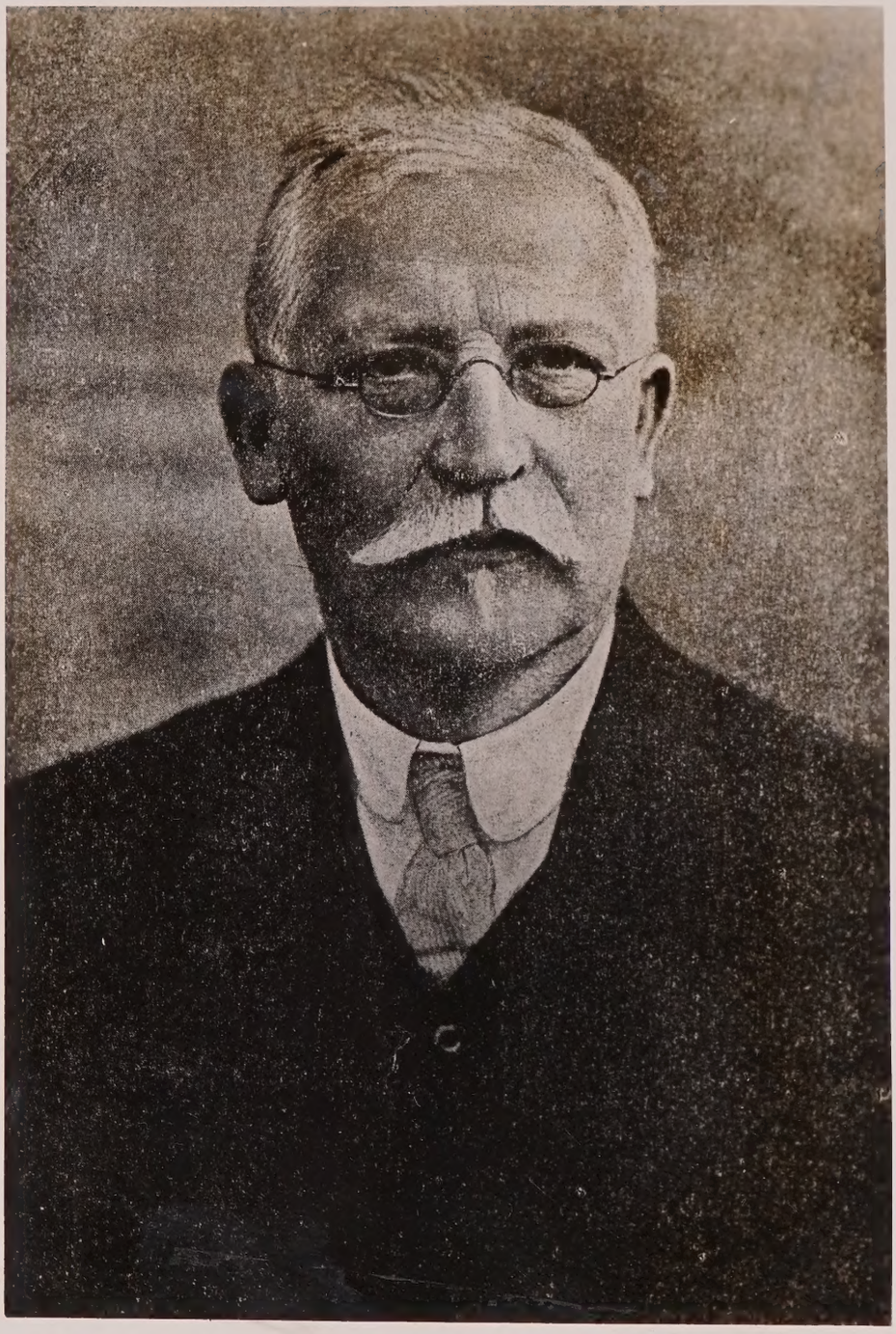
PETER BOROVSKY (1863-1932).
From a photograph taken in 1895.



Prof. P.F. BOROVSKY
Portrait taken in 1927

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INTRODUCTION.

The history of the discovery of the parasites causing oriental sore and kala-azar has already been discussed in a number of text-books of medical protozoology (*e.g.*, LAVERAN'S *Leishmanioses*, 1917 ; and WENYON'S *Protozoology*, 1926) and in some of the special papers dealing with the leishmaniases. The narrative given in different publications varies as regards both completeness and degree of accuracy, the latter depending upon the sources of information used by the writers and upon the interpretation of the available data.

In the case of oriental sore the first observer who actually saw the parasite, now known as *Leishmania tropica*, was CUNNINGHAM (1885) ; WRIGHT (December, 1903), however, is credited with the first correct description of this organism. Since the parasite of kala-azar, now known as *L. donovani*, was also discovered in the same year by LEISHMAN (May, 1903), the elucidation of both cutaneous and visceral leishmaniasis is generally associated with the year 1903. In LAVERAN'S important monograph on the leishmaniases this is emphasized in the opening sentence as follows : " La découverte des Protozoaires connus sous le nom de *Leishmania* ne date que de 1903 " (LAVERAN, 1917 : p. 1).

A few years ago PAWLOWSKY (1927, 1931) drew attention to the fact that the parasite of oriental sore was first correctly described and identified as a

protozoon in 1898, by a Russian military surgeon, P. F. BOROVSKY, whose observations were described in a memoir " On Sart Sore "* published in *Voenno-Medicinskij Žurnal*† [= Military-Medical Journal] (St. Petersburg), Part CLXXXXV, Book 11, November, 1898. This paper, being written in Russian, in a journal with a limited circulation, remained unknown outside Russia,‡ and even in the country of its origin BOROVSKY's discovery was not properly appreciated until quite recently (YAKIMOFF, 1915 ; PAWLOWSKY, 1927) though references to it and quotations from the paper appeared in some earlier publications (MARZINOWSKY and BOGROW, 1904 ; MARZINOWSKY, 1909, 1912 ; PETERSEN, 1912).‖

At present BOROVSKY's paper is available to readers not conversant with the Russian language only in the form of a short extract translated into German by PAWLOWSKY (1931). In Russia itself the journal in which the memoir appeared is now a bibliographical rarity, but part of the paper has been made accessible to a wider circle of Russian readers by the publication of extracts from it in commemoration of the 40th year of BOROVSKY's scientific career (ORLOV, 1927).

One of the objects of the present paper is to give an account of BOROVSKY's observations and to assign his discovery to its proper place in the history of tropical medicine and parasitology. Since the perusal of the original literature on the aetiology of the leishmaniases has revealed a number of new facts of historical interest, it is proposed at the same time to give a brief account of the work that preceded and followed BOROVSKY's discovery (with the exception of those investigations in which these diseases were attributed to bacteria).

The other object of this paper is to provide an unabridged English translation of BOROVSKY's memoir, thereby placing it in its entirety at the disposal of the English-reading public for the first time. In view of the inaccessibility of the original both because of its being out of print and because of language difficulties, it is hoped that future historians of medical zoology will be able to make use of this translation as an equivalent of the original text. To this end particular care has been taken to make the translation as literal as is consistent with correct English.

*" Sart sore " and " Pendeh sore " are two local names under which oriental sore is known in Turkestan. They are derived from the *Sarts*, a native tribe in the former Syr-Daria and Ferghana territories, and from *Pendeh*, a town in the former Transcaspian province, respectively.

†The transliteration is that adopted by the Russian Academy of Sciences. It has been used by me for names which have hitherto appeared in Russian only. For names of Russian authors who have employed other methods of transcription I have adhered to their own spelling.

‡Only brief and inadequate mention of BOROVSKY's discovery was made by PETERSEN (1912a) and by YAKIMOFF (1915a), the latter stating that " il a le mérite d'avoir reconnu, le premier, dans ces parasites des protozoaires." (*Loc. cit.*, p. 500.)

‖I have to acknowledge my indebtedness to Prof. W. L. YAKIMOFF, of Leningrad, for the loan of a number of reprints of Russian papers referred to above, which are unobtainable in this country.

I was unable to find the required issue of the " *Voenno-Medicinskij Žurnal* " in any of the scientific libraries of this country, but was fortunate enough to receive a copy of this rare publication from Prof. F. WALCKER, M.D., Director of the Library of the Military Medical Academy, Leningrad, to whom I wish to express my deepest gratitude for this service.

In addition to a review of the history of the discovery of the parasite causing oriental sore, I have appended a note dealing with the views of K. SHULGIN (1902) on the transmission of this disease. Although SHULGIN was the first to incriminate blood-sucking insects as vectors, his observations have passed almost unnoticed and remain practically unknown.

BOROVSKY'S PREDECESSORS.

The discovery of the causative agent of oriental sore is generally attributed to CUNNINGHAM (1885), who was certainly the first to devote his attention to other elements than the bacteria associated with the lesion, some of which were at that time believed to play a part in the production of the disease. In sections of a sore (" Delhi boil ") fixed in alcohol and stained with gentian violet CUNNINGHAM found numerous cells measuring on an average 12·6 by 8·8μ and varying in form. These cells contained rounded elements, referred to as " nucleoid bodies," which stained uniformly violet or blue, and varied in number and size. In some of the cells only " a single nucleoid mass " was present, in others " a few of very various sizes," while in others again " a large number of minute and fairly equal sized ones were thickly scattered throughout the entire cell."

CUNNINGHAM regarded these cells as " parasitic bodies " responsible for the disease, and referred them to the Mycetozoa or " slime-fungi." The cells themselves were believed to be the " parent plasmodia or amoebae " [= plasmodia] of a " Monadinic organism," while the " nucleoid bodies " within them were supposed to represent " sporoid bodies," or stages of development of " zoocysts or sporocysts " [= spores]. It is evident from the text that CUNNINGHAM had in mind a parasitic mycetozoon of the type of *Plasmodiophora*, to the plasmodial stage of which his figures bear some resemblance.

Amongst the elements described and depicted by CUNNINGHAM some, like the small " nucleoid bodies " of equal size, undoubtedly represented Leishman-Donovan bodies, while others—large single " nucleoid bodies " and cell-inclusions of unequal size—were either artifacts or products of degeneration.

It would thus appear that CUNNINGHAM was actually the first to have *seen* the parasites of oriental sore enclosed in the tissue-cells of the host, but he entirely misunderstood and misinterpreted their nature, for he regarded the host-cell (macrophage) as the parasite, while the leishmanias within it—which revealed no structure owing to the crude technique employed—were interpreted as spores developing in the parent plasmodium.

These findings were later confirmed by FIRTH (1891), who added nothing new to CUNNINGHAM'S description of the " parasitic bodies," but stated that

he " always regarded them as sporozoa and in 1887 went so far as to suggest . . . the name *sporozoa furunculosa* to indicate their peculiar pathological influence." In the legend to his Fig. 5 FIRTH refers to the elements evidently depicting the macrophages with enclosed leishmanias as " multinuclear bodies " which, he says, are " the spore-like bodies alluded to in the text." Since these bodies are also called " sporozoa " in the text, and " sporozooid bodies " in the title of the paper, it is clear that all these designations were regarded by him as equivalent.

I have dwelt on FIRTH's nomenclature at some length because certain authors have accepted " *sporozoa furunculosa* " as a binominal Linnaean name.* However, it is clear from the context and from the examples quoted above that FIRTH himself employed the name " *sporozoa furunculosa* " merely as a descriptive Latin medical term, the English equivalent of which would be *furunculous* (or *furuncular*) *sporozoa*, or—in the author's own words—" spore-like bodies " associated with boils. However, if formal arguments against the validity of FIRTH's nomenclature are required, it may be pointed out that the name *Sporozoa*, having been given to a class by LEUCKART in 1879, is not available for a genus ; furthermore, in the original text the name " *sporozoa*," though written in italics, begins with a small initial letter and appears in the plural form, with which " *furunculosa* " is in agreement. The last two items constitute an infringement of Art. 8 of the International Rules of Zoological Nomenclature, according to which " A generic name must consist of a single word . . . written with a capital initial letter, and employed as a substantive in the nominative singular."

BOROVSKY'S OBSERVATIONS.

BOROVSKY commenced his researches on the aetiology of oriental sore (" Sart sore ") in 1894 and published the results in 1898. He was fully conversant with the works in which the causative agent was sought amongst the bacteria, but evidently knew nothing about the publications of CUNNINGHAM and FIRTH. Though he also cultivated bacteria from the sore, he at once realized that they were of no aetiological significance and turned to the investigation of young, non-ulcerating sores.

He examined the " juice " from the sore in hanging drop preparations, made smears of the scrapings—fixed with absolute alcohol and ether and stained by Loeffler's method—and also cut and stained sections of excised sores after fixation in Zenker's fluid. In all these preparations he found numerous small spherical, oval or fusiform corpuscles, measuring about 1·5 to 2·0μ in diameter. In each of these bodies BOROVSKY distinguished a nucleus,† while in many he

*As far as I was able to ascertain, BLANCHARD (1904) was the first to insist on its validity.

†Curiously enough, MARZINOWSKY and BOGROW (1904a) and later MARZINOWSKY (1912), in their comments on BOROVSKY's work, erroneously imply that he failed to detect the presence of the nucleus.

detected a " process " running from the nucleus to the periphery of the body. In smears the parasites—for BOROVSKY immediately recognized the " corpuscles " as such—were either free or packed into " spheres," but in sections the majority were enclosed within the lymphoid or epithelioid cells of the host-tissues. Multiplication of the parasites was said to take place by simple fission, by a form of multiple division, and by budding. Attempts were made to cultivate the organisms, but these were unsuccessful.

BOROVSKY recognized the parasites as " unicellular organisms," which he referred to the " class of protozoa," and concluded that " Sart sore is not caused by any kind of bacteria, but by organisms of a higher order, *viz.* protozoa."

If BOROVSKY's data are examined from the point of view of our present knowledge, it will be seen that he not only gave an accurate description of the parasite of oriental sore,* but also established its true relation to the elements of the host's tissues. There can be little doubt that the " process " seen near the nucleus of the parasite represents the rod-shaped kinetoplast (=kinetonucleus),† while the " lymphoid " cells harbouring the parasites are evidently the macrophages.

To BOROVSKY thus belongs the credit of being the first to give a recognizable description of *Leishmania tropica*—and indeed of leishmanias in general—and of assigning it to the Protozoa.

It is inevitable that some minor errors of interpretation should have occurred in BOROVSKY's account, but if it is taken into consideration that his investigations were carried out independently, in a field in which he had no previous experience, it is surprising that these errors are so few and insignificant.

The foregoing is only a brief statement of BOROVSKY's findings. For full particulars of his investigations and for their interpretation the reader is referred to the translation of the paper " *On Sart Sore* " appearing in Appendix II, accompanied by the translator's comments. In addition to the observations leading to the elucidation of the aetiology of oriental sore, BOROVSKY has given a very accurate account of the clinical course and histopathology of this disease.

BOROVSKY'S SUCCESSORS.

BOROVSKY's investigations were closely followed by K. SHULGIN, his colleague at the Tashkent Military Hospital, who (SHULGIN, 1902) was soon able to confirm all BOROVSKY's results in the case of " Pendeh sore," which was prevalent in south-eastern Turkestan.

Though the history of the subsequent investigations on the aetiology of oriental sore is fairly well known, I have found—in the course of a careful study

*In this connexion it is interesting to note that YAKIMOFF (1915) had seen typical leishmania in one of BOROVSKY'S original preparations of oriental sore, made in the 'nineties and presented to YAKIMOFF in 1913.

†In BOROVSKY's Fig. 1 (see plate facing p. 84), depicting the parasites, this structure cannot be detected.

of the literature on this subject undertaken in connexion with the present inquiry—that a number of important data have been omitted or misinterpreted. In order to render this historical review as complete as possible, therefore, I propose to give a brief survey of the work leading to the establishment of *Leishmania tropica* in the position it now occupies.

While BOROVSKY was undoubtedly the first to give a recognizable account of this parasite, the details of its structure as it is known at present were first revealed by WRIGHT (1903). However, the actual description of the morphology of the parasite adds nothing new to BOROVSKY'S account, for WRIGHT refers to the nucleus and kinetoplast merely as " a larger and a smaller lilac-coloured mass " respectively, and only *assumes* that these structures " are of the nature of nuclei," whereas BOROVSKY definitely described the nucleus as such, and only failed to interpret the nature of the kinetoplast (his " process "). On the other hand, WRIGHT'S photomicrographs provide the first accurate illustration of the cytological details of the parasites in question. These were identified by him as Protozoa and tentatively referred to the Microsporidia, under the name *Helcosoma tropicum*. WRIGHT evidently knew nothing about BOROVSKY'S paper and (since he does not refer to them) it may be inferred that he was either unaware of the works on the parasite of kala-azar published in the course of the same year (1903) or did not appreciate their bearing upon his own investigation.

In 1904 there appeared two versions (Russian and German) of a paper by MARZINOWSKY and BOGROW (1904, 1904*a*) in which these observers give a correct description of the parasite of oriental sore, illustrated by photomicrographs. They refer to the nucleus and kinetoplast as macro- and micronucleus respectively, their interpretation thus coinciding with the conception of those authors who regarded the Trypanosomidae as binucleate organisms. They furthermore expressed their firm conviction that the parasite was a protozoon very closely related to *Trypanosoma*, though differing from it in certain characters. It is thus seen that MARZINOWSKY and BOGROW recognized the true affinities of the parasite of oriental sore, for which they proposed the name *Ovoplasma orientale*. Though the Russian authors arrived at this conclusion quite independently, BLANCHARD, whose paper appeared in May, 1904, was actually the first to draw attention to the close relationship of this parasite to the trypanosomes, but his opinion was based on the knowledge of LEISHMAN'S work on the parasite of kala-azar, as will be shown below.

It is not generally known that although MARZINOWSKY and BOGROW'S papers were published nearly a year later than WRIGHT'S, the investigations of the Russian authors and their conclusions were entirely independent of those of WRIGHT. This is clear not only from the dates appearing in the corresponding writings,* but also from the testimony of MESNIL (1904), who, in his review of WRIGHT'S paper, states that parasites identical with those described by WRIGHT

*The case described by WRIGHT first came under his observation on July 28th, 1903, while that which provided the material for MARZINOWSKY and BOGROW was examined by them between the end of May and the end of June, 1903.

(December, 1903) had already been seen by him in November, 1903, in preparations of an oriental sore received from MARZINOWSKY, a fact which is also recorded by the Russian observers (MARZINOWSKY and BOGROW, 1904*a*). From the work of these authors it is also obvious that, like WRIGHT, they had no knowledge of the preceding investigations on the aetiology of kala-azar. They were, however, familiar with BOROVSKY's memoir, but their paper shows a certain tendency to belittle his achievements, while some of his observations are even misrepresented (cf. footnote on p. 70). This attitude is also maintained by one of these authors in a subsequent paper (MARZINOWSKY, 1912).

The remaining publications on the parasite of oriental sore to be considered are those which led to the final elucidation of its morphology and to the determination of its systematic position as established at present. Attention has already been drawn to the fact that the investigations reviewed above were conducted independently and in ignorance of similar work carried out on kala-azar. However, the close resemblance between the causative organisms of this disease and of oriental sore was soon recognized, and thereafter the study of the two parasites began to be correlated. In order to understand the vicissitudes through which the classification of the parasite of oriental sore has passed, it is, therefore, necessary to make a digression and consider briefly the earlier work on the identity of the parasite of kala-azar.

When first discovered by LEISHMAN (1903) the parasite responsible for kala-azar* was referred to the trypanosomes and correctly described as possessing a macro- and a micro-nucleus [= kinetonucleus or kinetoplast]. LAVERAN (1903), however, concluded that this parasite represented a piroplasm and—with MESNIL—named it *Piroplasma donovani*. ROSS (1903) took the same view—though independently—as CUNNINGHAM did with regard to the parasite of oriental sore, and considered the entire host-cell (" matrix ") with the enclosed organisms, which he interpreted as " spores," to be the parasite, and referred it to the Sporozoa, emending LAVERAN and MESNIL's name to *Leishmania donovani*, under which it has been known ever since.

MESNIL (1904), who has made many valuable contributions to our knowledge of pathogenic protozoa in his critical reviews of the current literature, was the first to note the striking resemblance between *Helcosoma tropicum* and *Piroplasma donovani*, and suggested that the former should be placed " tout près des *Piroplasma*." The morphological similarity between the two parasites was confirmed by LEISHMAN (1904) and CHRISTOPHERS (1904), the former maintaining his belief in the flagellate nature of the parasite of kala-azar and the latter regarding it as a microsporidium. The position was then examined by BLANCHARD (1904), who pointed out that there was not a single character distinguishing the

*Though the Leishman-Donovan bodies were actually first seen by MARCHAND (1903), he did not consider them to be parasites, but regarded them as the product of degenerated cell nuclei. However, later MARCHAND and LEDINGHAM (1904) recognized that the structures previously observed by the first-named author were really the parasites described by LEISHMAN and others in 1903.

parasite of oriental sore from that of kala-azar and, accordingly, referred the former to the same genus under the name *Leishmania furunculosa* (Firth, 1891), in the belief that FIRTH's name "*sporozoa furunculosa*" was a valid binominal designation.* BLANCHARD followed LEISHMAN in admitting the possibility of *Leishmania* representing some stage of a trypanosome.

Shortly afterwards ROGERS (1904, 1904a) succeeded in cultivating *L. donovani* and demonstrating its flagellate stage. This observation led him to amplify LEISHMAN'S view and to regard the Leishman-Donovan bodies as a definite stage in the life-history of a trypanosome. MESNIL (1904a) attempted to reconcile his own views with those of ROGERS, on the basis of SCHAUDINN'S theory, by accepting two stages of development in the leishmanial parasite, one being an endoglobular piroplasm and the other a trypanosome. In a "Discussion on the Leishman-Donovan Body" at the 72nd Meeting of the British Medical Association, LEISHMAN (1904a) compared these bodies to the "resting forms" of *Herpetomonas muscae-domesticae*. A further step towards the recognition of the affinities of *L. donovani* with the insect-flagellates was made by MESNIL (1904b), who, in reviewing ROGERS'S paper on the cultural forms, stated that these were more like *Crithidia* or *Herpetomonas* than *Trypanosoma*. ROGERS (1906) arrived at the same conclusion and proposed to rename the parasite "*Hepatomonas* [obvious *lapsus calami* for *Herpetomonas*] of Kala Azar," a suggestion formally endorsed by MESNIL (1906) in emending the name to *Herpetomonas donovani* (L. & M.), the same amendment having been made later, but apparently independently, by PATTON (1908). The name of this parasite was again changed, to *Leptomonas donovani* (L. & M.), by MESNIL (1909).

In spite of all this evidence in support of the flagellate nature of the leishmanias, LÜHE (1906) in his systematic survey of the blood-inhabiting protozoa attached these parasites to the piroplasms. As far as I have been able to ascertain, this author was the first to adopt the name *Leishmania tropica* (Wright, 1903)† for the parasite of oriental sore, rejecting FIRTH'S name "*sporozoa furunculosa*‡ as invalid on account of its plural form (cf. p. 70). In conformity with *Herpetomonas donovani*, PATTON (1909) transferred the parasite of oriental sore to the same genus, under the name *Herpetomonas tropica*, but later he (PATTON, 1922) revived FIRTH'S designation and suggested the name *Herpetomonas farunculosa.*‖ Amongst the names given to this parasite the following should also be mentioned: *Leishmania wrighti* proposed by NICOLLE (1908a) and *Crithidium* [*sic*] *cunninghami* and *Leishmania cunninghami* by CARTER (1909). The last three names were introduced with an utter disregard of prior claims.

*The case against the validity of this name has been dealt with above (p. 70).

†This name was later suggested by WOODCOCK (1909), evidently in ignorance of LÜHE'S earlier amendment.

‡LÜHE erroneously attributed this name to CUNNINGHAM.

‖This spelling is an obvious *lapsus calami*.

The flagellate nature of *L. tropica* was demonstrated in cultures for the first time by NICOLLE (1908), thus finally establishing its morphological, if not specific, identity with *L. donovani*.

NOMENCLATURE OF LEISHMANIA.

As far as I am aware, the complete synonymy of *L. tropica* and *L. donovani* has never been published. The following revised lists, which contain all the names I have been able to trace under which these parasites have been described, can serve as a brief summary of the foregoing historical review.

(1) *Leishmania tropica* (Wright, 1903) Lühe, 1906 (*nec* Woodcock, 1909).

Synonyms :—

" Mycetozoa " Cunningham, 1885.
" *sporozoa furunculosa* " Firth, 1891.
" Protozoa " Borovsky, 1898.
Helcosoma tropicum Wright, 1903.
Leishmania furunculosa (Firth, 1891) Blanchard, 1904.
Ovoplasma orientale Marzinowsky & Bogrow, 1904.
Leishmania wrighti Nicolle, 1908.
Crithidium cunninghami Carter, 1909.
Leishmania cunninghami Carter, 1909.
Herpetomonas tropica (Wright, 1903) Patton, 1909.
Herpetomonas furunculosa (Firth, 1891) Patton, 1922.

(2) *Leishmania donovani* (Laveran & Mesnil, 1903) Ross, 1903.

Synonyms :—

Piroplasma donovani Laveran & Mesnil, 1903.
" *Hepatomonas* of Kala Azar " Rogers, 1906.
Herpetomonas donovani (Laveran & Mesnil, 1903) Mesnil, 1906 (*nec* Patton, 1908).
Leptomonas donovani (Laveran & Mesnil, 1903) Mesnil, 1909.

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APPENDIX I.

P. F. BOROVSKY (1863-1932): A BIOGRAPHICAL NOTE.

PETER FOKITCH BOROVSKY was born in 1863 at Pogar, in the Government of Chernigov, Russia. He studied medicine at the University of Kiev and at the Military Medical Academy in St. Petersburg, whence he graduated as an army doctor in 1887. Having specialized in surgery BOROVSKY obtained the degree of Doctor of Medicine in 1891 for a thesis entitled: *Contributions to the Study of Tuberculosis of the Bones and Joints* (St. Petersburg). In 1892 he was appointed to Turkestan, in charge of the Surgical Department and Bacteriological Laboratory of the Tashkent Military Hospital.

BOROVSKY'S early researches in Turkestan were devoted to the elucidation of the aetiology of " Sart sore," which is one of the local names for oriental sore. His work was conducted in a small laboratory with poor equipment, the most valuable of which, a Zeiss microscope with an oil-immersion lens, was BOROVSKY'S private property brought by him from St. Petersburg.

The results of these investigations were published by BOROVSKY in 1898, in a paper " On Sart sore," in *Voenno-Medicinskij Žurnal* [= Military-Medical Journal], in which he established the protozoal nature of the causative agent of oriental sore. Unfortunately, this work was destined to be BOROVSKY'S only incursion into the realms of protozoology, for at that period the demand for surgeons in Turkestan was so urgent that he was compelled to devote himself entirely to surgery. In the course of his subsequent career BOROVSKY, as Professor of Clinical Surgery in the State University of Middle Asia, was engaged in teaching, as well as in clinical and research work. He died in Tashkent,

where he had spent 40 years of his working life, on December 16th, 1932, at the age of 69.

The accompanying portrait (Frontispiece), taken in 1895, represents BOROVSKY—wearing the uniform of a medical officer in the Imperial Russian Army—at the age of 32, at the period when his researches on oriental sore were being conducted. The original portrait was given to the late Prof. G. H. F. NUTTALL, F.R.S., by Prof. E. N. PAWLOWSKY, of the Military Medical Academy, Leningrad, for inclusion in the "Portrait Gallery" of parasitologists at the Molteno Institute, Cambridge, and has been kindly placed at my disposal by Prof. D. KEILIN, F.R.S. The biographical data for this note were compiled from articles by I. I. ORLOV (*Pensée Méd. Uzbéquistane*, **2**, 1927, p. 5), E. N. PAWLOWSKY (*Ibid.*, p. 16), L. ISSAEV (*Med. Parasitol. & Parasit. Dis.*, Moscow, **1**, 1933, p. 277) and from two anonymous obituary notices (*Ibid.*, p. 287, and *Münch. med. Wschr.* **80**, 1933, p. 518).

APPENDIX II.

ON SART SORE.[1]

BY

P. F. BOROVSKY,

Junior House Surgeon, Bacteriological Department of the Tashkent Military Hospital.

p. 925 Sart sore is not widely distributed in Tashkent; it occurs only sporadically and new arrivals in the country do not invariably contract the disease as in the case of Pendeh sore, Aleppo boil, etc. The sores very rarely appear in the form of a multiple eruption; in most cases two or three sores occur, while solitary sores are not uncommon. Sart sore is thus more restricted in its distribution than Pendeh sore and its incidence amongst the troops is not of an epidemic character. Nevertheless, judging from the clinical and the anatomico-pathological pictures described by HEIDENREICH[2] and by RAPTSCHEWSKY, Sart sore is probably identical with Pendeh sore. It may therefore be assumed that the cause must be the same, though the conditions for the manifestation and spread of the infection are different. Moreover, in the Murgab valley itself the disease is not uniformly distributed, according to the investigations of RAPTSCHEWSKY (*Voenno-Medicinskij Žurnal*, 1889, Book VIII). HEIDENREICH and RAPTSCHEWSKY differ in their conclusions both as regards the cause of Pendeh sore and the method of its dissemination.

p. 926 On perusing both investigations one is forced to conclude that HEIDENREICH has investigated unsuitable old cases which had already become ulcerated, and that consequently the results obtained were doubtful. Thus,

[1] [*Published in*: *Voenno-Medicinskij Žurnal* (= *Military Medical Journal*), *St. Petersburg, November*, 1898, *Part clxxxxv, Book* 11 (*76th year*) *pp.* 925-941, 2 *text-figs.* (*In Russian.*)

Translated from the Russian text by C. A. HOARE.

The pagination of the original text is indicated in the margins; the annotations in italics between square brackets—both in the text and in the footnotes—are interpolated by the translator: those not distinguished in this way are found in the original.]

[2] [*In some publications this name is spelt "Heydenreich."*—C.A.H.]

HEIDENREICH[3] says : " if the end of a platinum wire is introduced into the fluid issuing from a scab subjected to pressure, and if a stab is made with this infected wire into sterile [*nutrient gelatin*][4] in a sterile test-tube it is sometimes possible, after several days, to obtain a culture of a special micrococcus." In view of this statement one can understand the scepticism regarding the " micrococcus Biskra, DUCLAUX et HEIDENREICH," especially since RAPTSCHEWSKY has obtained different results in his investigation. On account of the controversy regarding the aetiology of " oriental sore," and with the object of ascertaining whether Sart sore is identical with Pendeh sore, we undertook at the end of 1894 a bacteriological and anatomico-pathological investigation. The material for the investigation was provided partly by hospital patients and partly by out-patients. Most of the cases selected were in the early period, *i.e.* in the non-ulcerating stage, the importance of which was rightly pointed out by RAPTSCHEWSKY.

The investigation was carried out with long intervals owing to lack of suitable material. Frequently several months would elapse before a single suitable case was encountered, and this was due not so much to the rareness of the disease as to the fact that patients in the first period of the disease pay little attention to it, since at the beginning it causes no discomfort, and therefore in most cases they apply for assistance only during the period of ulceration.

THE CLINICAL COURSE OF SART SORE.

In the initial phase of its development Sart sore appears in the form of a nodule elevated above the surface of the skin and perceptible both to *p. 927* the eye and to the touch. The nodule, which is of a dark red hue, passes imperceptibly into the healthy tissue of the skin. Palpation is not painful ; the patient feels no discomfort, except a slight itching, and even this is not always experienced. After 10 to 20 days (we have not seen any earlier cases) there appears in the centre of the nodule a slight depression covered by a grayish, firmly adherent crust. On removal of this a small opening is revealed discharging a slightly turbid serous fluid. It is usually at this period that the nodules begin to ulcerate, starting from the centre, while an infiltration spreads into the surrounding healthy tissues.

When kept clean and in the absence of external irritation the nodule does not ulcerate, but begins to increase more or less regularly, sometimes assuming the appearance of a plaque about 4 to 5 cm. in diameter, while the skin takes on a bluish tint and its surface becomes considerably desquamated. Sometimes in the infiltrated area of the skin the papillae begin to proliferate and the surface becomes covered with numerous minute papillae. The papillae are more defined in the centre, diminishing towards the periphery, while at the edge the

[3]L. L. HEIDENREICH : Pendeh Sore (Tropical Sore). Attacks, cause, identification, etc. Publ. by Chief Milit. Med. Dept. [*St. Petersburg*, 1888. (*Review in : Ann. Inst. Pasteur*, **3**, 1889, 445.)]

[4][*In the original only the initials, indicating " meat-gelatin," are given.*—C.A.H.]

skin is smooth. The margins of the area of infiltration are slightly raised above the middle : between the papillae there is an accumulation of desquamating epithelium, and in some places there are small fissures discharging a slightly turbid fluid.

In Sart sore the infiltration is continuous and individual nodules are not palpable.

Large papules are, however, comparatively rare ; in most cases after 2 to 3 weeks a superficial ulcer is produced with a slightly eroded edge ; the discharge from the ulcer is not copious and a crust is, therefore, easily formed ; around the ulcer the infiltration area assumes a bluish-red hue and has a doughy consistence on palpation. We have never had the opportunity of seeing the lymph nodes in the course of Sart sore ; in general this symptom[5] (which is, according to RAPTSCHEWSKY, a complication of the sore) does not occur in the Sart sore of Tashkent.

The rate at which Sart sore spreads varies in different parts of the body. If the disease appears on the nose, the eye-lids, or the face in general, the infiltration increases far more rapidly.

p. 928 We have not observed natural healing and therefore possess no data for judging how long the sore can last ; we have, however, observed several sores of more than a year's duration which had to be treated before they healed.

As regards the situations in which the sores appear, our observations confirm those of previous observers, *viz.* that the sore mainly attacks the exposed parts. But whereas in our cases the sores occurred most frequently on the face, according to RAPTSCHEWSKY, HEIDENREICH and others, the shin and forearm were the parts most frequently affected, and the face only to a lesser degree.

As to the time of year when the incidence of the disease is highest, in Tashkent the greatest number of cases appear in January, February, March and April, and then in November and December, while there are considerably fewer cases during the summer months.

The incidence of the disease is higher among the lower classes of the population, though cases also occur among the well-to-do.

Sart sore heals with the formation of a superficial, slightly depressed, flat cicatrix ; this is at first of a darker colour, but as time passes it becomes paler and remains whiter than the surrounding parts.

As regards the diagnosis, it is difficult to confuse the sore with anything else if its development is taken into consideration.

We realize that ordinary ulcers of the shin and those which frequently affect the nose might give rise to doubts. However, in the first case cleanliness and rest rapidly produce an amelioration leading to cicatrization of common ulcers, whereas Sart sore remains for weeks in the same state under similar conditions ; moreover, if attention is given to the appearance of the area of

[5] [*Viz., enlargement of lymph nodes due to lymphangitis* : *cf.* HEIDENREICH, 1888 (*abstract in Ann. Inst. Pasteur*, **3**, 1889, *p.* 445).—C.A.H.]

infiltration—its doughy consistence, indolence, the bluish-red hue of the skin above the infiltration—its identification presents no difficulties. It is sufficient to see the sore once or twice to be able to diagnose it without error.

As regards the lesion on the nose this may at first lead to confusion with lupus, but the doughy consistence and the more diffuse character of the infiltration in the case of Sart sore, the absence of minute nodules separated from the main focus by healthy patches of skin, are sufficient for the differentiation of these disorders, apart from the difference in the rate of spreading. As *p. 929* stated above, Sart sore spreads rapidly over the whole nose, whereas in lupus the process is much slower. In the later stage of development it is impossible to confuse the two diseases since lupus destroys the cartilage and bone, whereas Sart sore never penetrates beyond the skin.

PATHOLOGICAL ANATOMY.

The earliest period at which we had occasion to examine a sore was after 2 weeks. The following are the changes observed : There are no special changes in the epidermal layer ; the Malpighian epithelial layer is already slightly altered —in the centre of the papule the interpapillary projections of the Malpighian layer are shorter than at the periphery and in places the granulation tissue penetrates through them in the form of rounded rods. The chief changes, however, occur in the dermis. The dermal papillae are permeated with the granulation elements, mostly in the form of epithelioid cells ; the proliferation of the granulation tissue proceeds mainly along the vessels. The accumulation of cells is greatest in the centre of the papule, resulting in the formation of an area of dense infiltration, while towards the periphery the islets of granulation tissue are separated from each other by areas of more or less modified connective tissue. In the deeper parts of the corium, where it passes into the subcutaneous connective tissue, are scattered accumulations of granulation elements in the form of isolated foci, which are also situated around the vessels. These deep accumulations of cells are separated from the more superficial ones by a thick layer of unaltered or slightly altered connective tissue. The blood-vessels are altered even at this early stage of development of the sore : the endothelium is swollen, inside the vessels there are accumulations of white corpuscles ; the minute arteries and veins are not infrequently narrowed to the point of disappearance of the lumen, partly owing to the accumulation of lymphoid elements around them, and partly to changes in their walls.

In the papular stage the cellular infiltration is more marked in the reticular layer of the dermis than in the papillary layer. In the course of its further proliferation the granulation tissue approaches the surface, progressively *p. 930* disrupts and destroys the Malpighian epithelial layer, raises the epidermal layer and, having destroyed the latter at some point, spreads over the surface. For this reason it is not uncommon to encounter an entire strand of epidermis as well as of the Malpighian layer in the midst of the granulation tissue, whereas

at the periphery, where there is less infiltration of the cellular elements, there can be observed a considerable thickening of the epithelial layer, the interpapillary projections of the epithelium not infrequently branching and the boundary between the epithelium and the surrounding tissue not being sharply defined. This phenomenon has, however, long been noted in all kinds of chronic ulcerative processes of the skin. During the period of ulceration the changes in the vessels are more marked: the walls of the minute arteries and veins are infiltrated, the vessels in some parts being occluded. In the midst of the granulation tissue there occur free accumulations of red blood corpuscles, either still retaining their appearance or already having broken up and formed rounded or irregular yellow accumulations; such accumulations are scattered in different parts of the ulcer and also occur in the epithelial layer.

During the period of ulceration the granulation tissue undergoes further development in some parts and is transformed into connective tissue with a small number of spindle-shaped cells, this transition taking place in the more superficial layers, whereas from the deeper parts there develops a thick layer of granulation tissue.

AETIOLOGY.

The cause of Sart sore and of other similar (if not identical) "oriental sores," such as Pendeh sore, Aleppo boil, [*bouton de*] Biskra, the Elisabethpol "godovik"[6] etc., has not been firmly established up to the present.

Duclaux, Heidenreich and Chantemesse investigated the "bouton de Biskra" in 1884 and isolated in culture a micrococcus similar to (if not identical with) the golden staphylococcus [=*Staphylococcus aureus*].

p. 931 Heidenreich, who studied Pendeh sore in 1886, confirmed Duclaux's investigation, *viz.* he attributed the origin of the sore to the penetration into the skin of "micrococcus Biskra," which is apparently identical with the golden staphylococcus.

Dr. Raptschewsky, who investigated Pendeh sore after Heidenreich, obtained different results: on examining the juice of the papules he isolated a streptococcus which differs from that of erysipelas and which he regards as the causative agent.

Nicolle and Noury-Bey have carried out a bacteriological investigation of Aleppo boil (*Annales de l'Institut Pasteur*, 1897, No. 9) and have also isolated a streptococcus which they regard as the causative agent. These authors studied nine cases: in three they obtained a pure culture of streptococcus, in five cases staphylococci developed together with the streptococci, and in one case bacilli were also present. Clinically Aleppo boil runs the same course as Sart sore and Pendeh sore: at the beginning there appears a papule of the size of an acne [*pustule*] which gradually increases in size; the papule is indolent and the

[6] [*godovik* = (*lit.*) *annual*: *name for the Transcaucasian form of oriental sore, which usually persists for* 1 *year*.—C.A.H.]

colour of the skin remains unchanged ; by the 3rd to the 5th month the papule becomes covered with a crust under which there is an ulcerated bleeding surface ; the pathological process extends further, there is an exudation of a sero-purulent fluid, and 3 to 4 months later cicatrization begins. According to NICOLLE and NOURY-BEY, the entire period of development of Aleppo boil is 11 to 12 months.

However, the species of streptococci isolated by RAPTSCHEWSKY and by NICOLLE and NOURY-BEY are different. RAPTSCHEWSKY'S streptococcus is distinguished by slow growth : the colonies cultivated on agar-agar at the optimum temperature (30 to 36°) become visible to the naked eye only on the 3rd or 4th day in the form of small whitish discs. On gelatin their growth is still slower ; the streptococcus does not liquefy gelatin ; in stab cultures growth takes place only along the course of the stab, without any signs of growth over the surface. When grown in fluid nutritive media the streptococcus forms a fine white precipitate. The streptococcus isolated by NICOLLE and NOURY-BEY is characterized by rapid growth in all kinds of media : the development of the colony can be noticed even after 24 hours ; when growing in broth the streptococcus produces a golden-yellow colour.

From the foregoing it is obvious that there is a complete difference of opinion regarding the aetiology of " oriental sore." Before turning to the results of our own research, we shall give an account of the method of *p. 932* investigation.

If the patient was in hospital, the sore was dressed for several days with warm boric acid compresses ; then the papule was washed with alcohol and ether, after which it was excised and removed with instruments boiled in a solution of soda. A scraping was then immediately taken from its deep bleeding surface with a sterilized knife. By means of a platinum loop passed through a flame this scraping was transferred to gelatin or agar-agar which was poured out into Petri dishes ; or the superficial layers of the sore were removed with a sharp spoon, while with a second spoon scrapings were made from the deeper parts and were used for making smears on slides and for inoculation. The excised portions of the papules, and sometimes of the ulcers, intended for an anatomico-pathological investigation were first hardened in 95 per cent. alcohol and then embedded in celloidin for the preparation of sections. The very first cases studied by us produced unexpected results : streptococci were not obtained in cultures but in their stead there developed a small number of yellow and white staphylococcus colonies and sarcinae, the number of bacteria being so insignificant that in the second and third cultures only a few isolated colonies developed, in view of which we made only one culture in subsequent cases. Moreover, in smears from the juice of the papules microorganisms were either absent or only solitary cocci were encountered.

From the end of 1895 we began to examine the juice of papules and sores in which no inflammatory phenomena were manifested, in hanging drops, and were astonished by the presence of numerous motile corpuscles, some round,

some irregular, while some of them possessed pseudopodia.[7] Since that time and up to the present we have found the same structures every time we have examined the juice and scrapings from the sores.

The younger the papule the greater was the number of these corpuscles, whereas only a few of them were present in scrapings from the depth of the older sores. At the beginning, when we dried and fixed the smear directly over the flame, according to the method usually adopted, the examination of the smears gave negative results. Recently, however, when we proceeded
p. 933 to fix the smears with a mixture of absolute alcohol and ether, staining with Loeffler's solution revealed the same corpuscles which had been observed in the hanging drop. The size of these structures varies from $\frac{1}{2}\mu$ to 2μ, occasionally reaching 3μ, but in most cases their dimensions are from $1\frac{1}{2}$ to 2μ. These corpuscles frequently have a fine process as long as, or sometimes longer than the diameter of the corpuscle ; at the end of the process there is not infrequently a small globular thickening ;[8] sometimes several—two and three—of these processes are observed. The corpuscles described are colourless : they are sometimes homogeneous, or they appear to have a nucleus in the centre or at the periphery, while in some of them vacuoles can be seen.[9] Moreover, in the hanging drop are observed minute dark structures of a round shape with one or several fine processes ; the latter structures are very motile.[10]

The shape of the corpuscles is sometimes spherical and sometimes fusiform. Occasionally a change in their shape could be observed—an oval would change into a sphere, then into an irregularly-shaped body and afterwards again become oval.[11] In two cases spheres were observed measuring 4 to 5μ, having a double-contoured membrane and densely packed with round corpuscles. One such sphere was seen to be half empty, while in the other half the round corpuscles were also disposed outside the membrane.[12]

If a hanging drop preparation was left in a thermostat it showed considerable changes after 24 hours : the larger round bodies disappeared and broke up, while the number of the above-mentioned minute structures with fine processes increased.[13] If the preparation was pure, all the structures disappeared after

[7] [*It is possible that some of these " corpuscles " may have been blood platelets and that the motility refers to Brownian movement.*—C.A.H.]

[8] [*The appearance of the " corpuscles " described here would suggest that in some of the parasites only the nucleus and rod-shaped kinetoplast were visible, a not infrequent occurrence in poorly fixed tissues.*—C.A.H.]

[9] [*These cases probably refer to the whole parasite.*—C.A.H.]

[10] [*V. supra: footnote* 7.]

[11] [*The apparent change of shape can be accounted for by the different views of the parasite, obtained in the course of its slow revolution.*—C.A.H.]

[12] [*These " spheres " represent detached fragments of the cytoplasm of the host-cells. They have been described by other authors, some of whom have regarded them as representing the parasite itself, while the true parasites were mistaken for its " spores "* (CUNNINGHAM, 1885 ; FIRTH, 1891 ; and ROSS, 1903 : *the last in the case of kala-azar*).—C.A.H.]

[13] [*V. supra: footnote* 7.]

2 or 3 days, whereas in the case of contamination with bacteria the latter, which were chiefly cocci, developed.

On examining sections of preparations fixed with 95 per cent. alcohol and stained, according to RAPTSCHEWSKY'S directions, with Loeffler's solution we never found any streptococci, but there were masses of what at first appeared to be cocci, some round, but most of them oval, arranged in clumps which were frequently spherical.[14] These cocci were in most cases packed in the protoplasm of the lymphoid and epithelioid cells.[15] In some cases after inoculation from excised papules the plates remained sterile, although an examination of the sections revealed a large accumulation of the cocci in question, while in *p. 934* the hanging drop the above-mentioned corpuscles were always observed in large numbers.

At the end of 1897 we began to employ for fixation Zenker's fluid, the composition of which is as follows:—Aq. destillatae 100·0, corrosive sublimate 5·0, potassium bichromate 2·5, sodium sulphate 1·0, acetic acid 5·0.

A freshly excised piece was dropped into this fluid and left there for 12 to 24 hours, after which it was washed for 24 hours in water and then transferred to 60 to 70 per cent. alcohol, absolute alcohol, absolute alcohol + ether, and embedded in celloidin.

After fixation with this fluid we succeeded in discovering in sections masses of corpuscles of the same size and shape as we had observed in the hanging drop.

The younger the papule of Sart sore the greater the number of these corpuscles ; the older the papule, or if in the period of ulceration, the fewer these corpuscles; and finally, in old papules with extensive ulceration or in those treated by cauterization, we found them with difficulty and even then in an altered state.

The fresh papule presents the following picture : these corpuscles are absent in the epidermoid and epithelial layers, and are rare in the papillae ; the parasites, in most cases enclosed within cells, only make their appearance where the infiltration rises from the deeper layers of the skin to the papillae ; the parasites are most numerous in the deeper parts where the accumulation of granulation cells is the greatest. The cells are literally packed with them to such an extent that the limits of the individual parasites cannot be seen, and they appear as one continuous mass in which only their nuclei, stained deeply with Loeffler's solution, are distinctly visible. This is the reason why the earlier preparations produced the impression that these accumulations consisted of cocci. However, deeper down, towards the subcutaneous connective tissue, the accumulations of parasites become less abundant and it is here that they can be observed *p. 936* individually. They proved to be mostly round corpuscles (though some are

[14] [*When the nuclei only of the parasites are visible, an appearance of masses of cocci is produced. However, as will be seen below, the author was fully aware of the true nature of these "cocci."*—C.A.H.]

[15] [*This is the first correct interpretation of the nature of the parasitized host-cells.*—C.A.H.]

oval and spindle shaped) with a very faintly stained protoplasm and a sharply stained nucleus situated at the periphery. This nucleus is either round or elongated in shape, while sickle-shaped nuclei are also not uncommon.

As mentioned, these parasites are in most cases situated within cells, the nucleus [*of which*] is shifted to the periphery, stains badly and is shrivelled, or sometimes destroyed, a cluster of parasites being seen in place of the cell. Accumulations of parasites also occur outside the cells. In such cases there are encountered spheres filled with round corpuscles with a feebly stained protoplasm and a nucleus at the periphery.

Still deeper, where there is no infiltration with the lymphoid elements, in the fissures between bundles of connective tissue and in the perivascular spaces, there can be seen rows and small clumps of the same parasitic cellular structures.

The size of the parasites is in most cases about 1μ, sometimes larger, but rarely smaller. Their nuclei vary in dimensions; sometimes they occupy a considerable part of the whole body, and not infrequently there can be seen a fine process running from the nucleus to the opposite side of the body, the process bearing a small globular thickening.[16]

On examining a papule, in which a small ulceration covered with a crust has already been formed, it is seen that the cellular infiltration, having reached the surface of the epithelial layer, has destroyed it and spread over the surface. The infiltration penetrates into the depth and spreads widely, while the parasites together with the granulation elements break their way outwards, though they are considerably less numerous on the surface than in the deeper parts.

On the other hand, the accumulations of lymphoid elements scattered in the subcutaneous connective tissue also contain smaller numbers of the parasites.

Amongst the accumulations of blood found at the bottom of the ulcer are seen considerable numbers of parasites which are occasionally situated within the red blood corpuscles.[17]

Several times, on examining the juice of the papules in a hanging drop, we
p. 937 have observed the parasites inside the red blood corpuscles, the parasite changing its position and shape. In sections the greatest accumulation of parasites occurs around the vessels where, as already stated, the infiltration is also greatest.

The oldest papule examined by us was about 1 year old. This case had been treated by repeated applications of tincture of iodine. In this instance most of the granulation tissue had passed into the connective tissue and only small accumulations of lymphoid elements were encountered in different parts of the section. The parasites could be detected with difficulty and had undergone alterations: they stained uniformly and most of them had bud-like outgrowths.

[16] [*This description evidently refers to the whole parasite in which the nucleus and elongated kinetoplast* (" *process* ") *were seen.*—C.A.H.]

[17] [*Misinterpretation of superimposed position of the parasites. The same error was committed by a number of authors in the case of* Leishmania donovani (Laveran, 1903; Laveran & Mesnil, 1903; Leishman, 1903).—C.A.H.]

Рис. 1. Разрѣзъ изъ 2-хъ недѣльной папулы при увелич. 37; болѣе темныя мѣста указываютъ мѣста скопленія грапуляціонныхъ элементовъ.

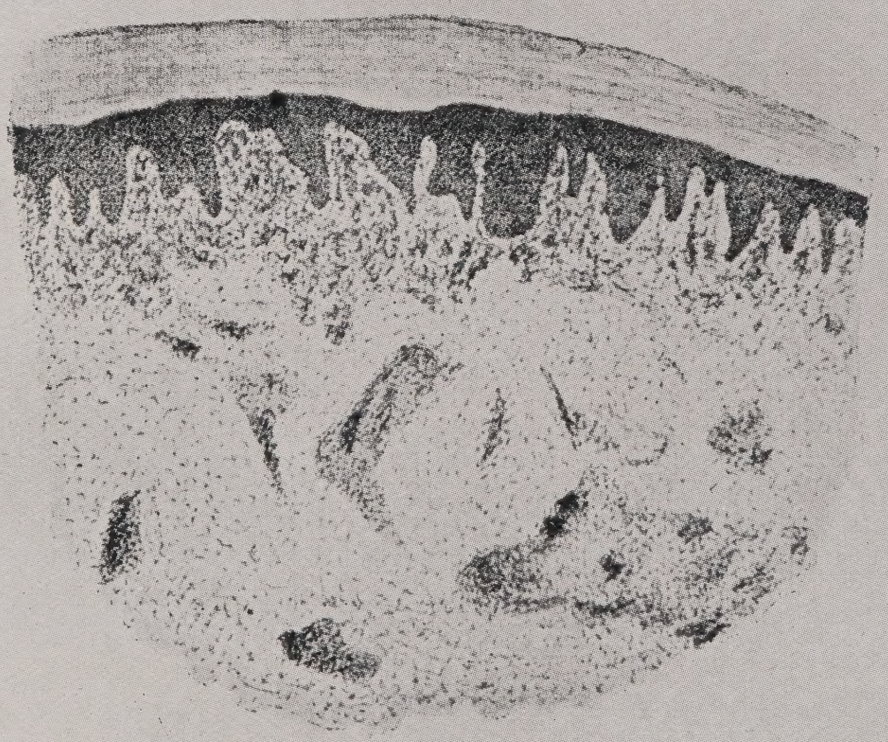

Рис. 2. Тотъ же препаратъ. при увеличеніи 1500 (Масл. сист.); въ центрѣ разрѣзъ кисты, наполненной чужеядными.

FACSIMILE OF PAGE 935 IN BOROVSKY'S MEMOIR.

Legend to Figures.

(*Translated from the Russian.*)

FIG. 1.—Section from papule 2 weeks old, at a magnification × 37 : the darker places indicate the areas of accumulation of granulation elements.

FIG. 2.—The same preparation at a magnification × 1,500 (oil immersion) : in the centre is a section of a cyst filled with parasites.

[*As in the original article, the arrangement of the description is reversed, Fig.* 1 (*top*) *bearing the legend of Fig.* 2 (*bottom*), *and vice-versa.*—C.A.H.]

To face page 86

Что касается нашего изслѣдованія, то данныя, полученныя нами, слѣдующія:

1) Въ сокѣ папулъ и не воспаленныхъ, еще не старыхъ язвахъ всегда находятся одноклѣточные организмы, которые, повидимому, должны быть отнесены къ классу «protozoa».

2) При посѣвахъ сока язвъ вырастаютъ различнаго вида бактеріи и то въ небольшомъ количествѣ, а иногда посѣвы остаются безплодными.

3) Присутствіе въ мазкахъ и срѣзахъ изъ папулъ множества тѣхъ же организмовъ, какіе наблюдаются и въ висячей каплѣ.

4) Обнаруживается масса «protozoa» въ раннемъ періодѣ развитія язвы и уменьшеніе и даже полное исчезновеніе въ очень старыхъ язвахъ; отсутствіе въ то же время какихъ либо дробянокъ въ ранней степени развитія язвы и увеличеніе ихъ количества въ старыхъ язвахъ, изъязвленныхъ, которыя, какъ это отмѣчено всѣми наблюдателями, приближаются къ простымъ язвамъ.

На основаніи всѣхъ этихъ данныхъ мы приходимъ къ заключенію, что сартовская язва вызывается не видомъ какихъ-либо дробянокъ, а организмами болѣе высшаго порядка, — protozoa.

FACSIMILE OF PART OF PAGE 939 IN BOROVSKY'S MEMOIR.

General conclusions, corresponding to pp. 88-89 of the Translation.

To the above it may be added that no schizomycetes could be detected in the non-ulcerating papules by staining.

The parasites described by us stain with Loeffler's solution, the sections being kept in the stain from 2 to 24 hours. Good staining can also be obtained with a saturated aqueous solution of safranin, but the parasites do not stain by Gram's method. We also tried to stain sections by Romanowsky's method (a mixture of eosin and methylene blue) and by the method of Sanfelice, as recommended by the latter for blastomycetes, but though they stained the staining was not sharp. The best method, therefore, is to stain with Loeffler's methylene blue solution followed by rinsing in water and decolorizing in alcohol, but the differentiation should not be carried too far: the same refers to the staining with saturated aqueous solution of safranin.

We failed to obtain cultures of the structures described: inoculations were made into the fluid obtained by puncture of a hydrocele, on agar-agar mixed with ascitic fluid, and in sterile grape juice.

Owing to the peripheral position of the nucleus and to the presence of processes like flagella,[18] we are inclined to refer the parasites described by us to the class of protozoa. Their multiplication apparently takes place both by means of direct division and by budding. We have observed corpuscles in which a short round outgrowth or bud is formed on the periphery, therefore multiplication by budding takes place,[19] though round corpuscles in which a fine process with *p 938*
a thickening at the end is given off from the nucleus occurred more frequently.[20] There also occurred corpuscles with two nuclei situated at opposite ends of the body. As the result of slow multiplication there may thus be produced several separate corpuscles enclosed in a common membrane, as was observed by us[21]; whereas in the course of rapid multiplication the division of the nucleus

[18] [*Vide infra: footnote* 20.]

[19] [*It is not improbable that the budding forms represent some yeast-like organism which may be present in ulcerating sores and bear some resemblance to* Leishman-Donovan *bodies when stained* (*cf.* WENYON, 1926, *p.* 428). *The latter interpretation receives support from the fact that a yeast was actually cultivated by the author from sores* (*cf. p.* 88).—C.A.H.]

[20] [*The presence of a "process" in the parasite is mentioned four times in the text* (*cf. footnotes*: 8, *p.* 84; 16, *p.* 86; 18, *supra*). *According to* BOROVSKY, *it arises from the nucleus, runs to the opposite side of the body and is provided with a "globular thickening" at the end* (*there is no indication as to whether it is at the proximal or distal end of the "process"*). *It is obvious that* BOROVSKY *must have seen the kinetoplast, either alone or together with the rhizoplast. In the former case the whole "process" would be equivalent to the kinetoplast, in the latter case the "globular thickening" alone would represent this structure, the "process" itself being the rhizoplast.* BOROVSKY *himself likened the "process" to a "flagellum," but the indications in the text suggesting that in some cases he must have seen only the nucleus of the parasite with the attached "process," coupled with the fact that the kinetoplast always stains deeply and is, therefore, more commonly seen in preparations of the* Leishman-Donovan *bodies than the rhizoplast, are strong arguments in favour of regarding* BOROVSKY'S *"process" as the kinetoplast. This is the view held by* PAWLOWSKY (1927, 1931); *and* Dr. C. M. WENYON, *whom I have consulted on this matter, is of the same opinion.*—C.A.H.]

[21] [*A condition interpreted by some authors as multiple division.*—C.A.H.]

is followed by fission of the protoplasm and separate individuals are produced. It is difficult, of course, to form an exact idea of the method of multiplication from a dead preparation, and not from a pure culture, therefore the account given above represents a personal impression.

In old Sart sores the parasites described are very scanty and they are, moreover, modified—thus there occur round corpuscles similar to those described above in size, but either uniformly stained or in the form of a transparent vesicle only the outline of which is visible. Even when those with nuclei are encountered, the nucleus is considerably smaller than usual and not so deeply stained as in the case of preparations from young papules.

In addition to what has been said above, it must be stated that, up to the present, inoculations from the Sart sores examined were made in Petri dishes and colonies were obtained of staphylococci (most frequently) and sarcinae; moreover, in three cases there developed very minute oval cocci which did not liquefy gelatin and, when examined in the living condition, were mostly arranged in pairs, in the form of diplococci; in one case there appeared in a Petri dish with agar-agar five colonies of microc.[*occus*] tetragenus; and in another case there developed amongst other colonies pink yeasts, while in two cases the plates remained sterile. The total number of cases examined by us exceeded twenty, nine of which were still in the form of papules.

Of course, we cannot yet extend the results obtained from the investigation of Sart sore to other similar diseases of the skin, such as Pendeh sore, Aleppo boil, [*bouton de*] Biskra, Elisabethpol " godovik "[22], etc., but would suggest the desirability of verifying their nature from the point of view put forward by us. The desirability of this verification is based on the following facts. In his study of Pendeh sore, RAPTSCHEWSKY makes the following statement: " in
p. 939 spite of repeated investigations, the result of bacterioscopic examinations of the ' lymphangitic ' nodules[23] in cases of Pendeh sore remained negative. It was impossible to detect any microorganisms in the juice mixed with blood obtained from incised nodules, either microscopically or by means of cultures."

However, in another place RAPTSCHEWSKY mentions that under the influence of irritation such a " lymphangitic " nodule may suppurate, open and then heal, like an ordinary abscess; and, further, that these complications in the form of lymphangitis occur in the case of sores which are contaminated or irritated, and in which there is a retention of pus under the crust. If that is the case, why are there no microbes in the " lymphangitic " nodules? However that may be, it is impossible to decide anything *a priori*.

As regards our own investigation, the data obtained by us are as follows:—

(1) In the juice of papules and in sores which are not yet old and have not ulcerated, there are always present unicellular organisms which should apparently be referred to the class " protozoa."

[22] [*Cf. Footnote* 6, *on p.* 82.]

[23] [*These are evidently the lymph nodes affected by lymphangitis.*—C.A.H.]

(2) In cultures of the juice from sores there grow various kinds of bacteria, though in small numbers, but sometimes the cultures remain sterile.

(3) In smears and sections of papules there are present large numbers of the same organisms which are observed in the hanging drop.

(4) Masses of " protozoa " are encountered in the early period of development of the sore, diminishing and even disappearing completely in very old sores. At the same time bacteria of any kind are absent in the early stages of development of the sore, but they occur in increasing numbers in old ulcerating sores, which, as has been noted by most observers, approximate to ordinary ulcers.

From all these data we arrive at the conclusion that Sart sore is not caused by any kind of bacteria, but by organisms of a higher order, *viz.* protozoa.

As regards the method of infection, we are inclined to think that the infection does not penetrate into the skin directly, but is conveyed either from the intestinal tract or from the respiratory apparatus through the blood. *p. 940*

The fact that exposed parts of the body are affected by preference can be explained by the greater susceptibility of these parts to traumata and to the appearance of minute capillary haemorrhages in which the accidentally transferred parasites find a suitable material [= *medium*] for development. Owing to the low toxicity of the products of metabolism of these parasites the phagocytes overcome them with comparative ease, and although many of the phagocytes perish, they appear in ever increasing numbers and finally destroy the parasites. That protozoa can find their way into the respiratory tracts has been proved experimentally. Thus, GRASSI and FELETTI demonstrated the presence of an extremely minute amoeba in the nasal cavities of pigeons which remained for two nights in a marshy locality at an altitude of 2 metres above the level of the ground, while 9 days later the same amoebae were found in the blood of the pigeons (LAVERAN et BLANCHARD, *Hématozoaires du Paludisme*). Infection with marsh fevers also takes place through the respiratory tract. Infection through the intestinal tract is possible through water and, it may be, through contaminated food.

As regards water used for washing and bathing, the transmission of infection through this medium is very doubtful, since, in spite of the fact that during the summer heat the entire Russian population of Tashkent bathes in " aryk " water[24], cases of this disease are very rare in summer. According to our observations, cases occur more frequently during the winter and spring months of the year. The last circumstance also shows that the rôle of dust in the spread of the disease is insignificant (if indeed it serves as a vector of the infection at all), for during the said time of the year the rainfall in this locality is very heavy.

TREATMENT.

In Tashkent the most commonly used remedy for the treatment of Sart sore is pure lactic acid, which is employed either in an ointment or in a layer of *p. 941*

[24] " Aryki " [*pl.*] are shallow canals by which water is conveyed for the irrigation of gardens, kitchen-gardens and fields [*in Turkestan*].

cotton wool impregnated with it and applied to the sore, where it is left for 24 hours. The latter method is more reliable ; when it is used the healthy skin around the sore is covered with collodion or an adhesive plaster. After 24 hours the dressing is removed and in place of the previous infiltration a scab is formed under which is a clean ulcerated surface, which is usually treated as an ordinary ulcer.

When the ulcer is cauterized successfully in this manner it heals in the course of 2 to 4 weeks. We have also applied the sublimate ointment recommended by Dr. TEKUTIEV with satisfactory results.

However, in some cases the infiltration re-appeared after cauterization and subsequent cicatrization ; in these cases we scraped it thoroughly with a sharp spoon. Scraping was also practised in cases where the eyelids were affected and cauterization could not be employed. A thorough scraping was always followed by healing.

When the papules were excised right down to the subcutaneous connective tissue, we inserted a suture which in most cases resulted in complete healing *per primam intentionem*, though sometimes under the cicatrices a fresh lesion would occur, necessitating either cauterization or scraping.

APPENDIX III.

K. SHULGIN (1902) : ON THE TRANSMISSION OF ORIENTAL SORE.

It has already been mentioned (p. 71) that K. SHULGIN, who was BOROVSKY'S contemporary at the Tashkent Military Hospital, fully confirmed his colleague's observations on the aetiology of oriental sore. However, SHULGIN'S real claim for a place in the history of tropical medicine rests on the views he expressed regarding the transmission of this disease, for he was actually the first to suggest, in 1902, that the vector was a blood-sucking insect. The part played by SHULGIN in enunciating this hypothesis is practically unknown to anyone, either in his own country or outside it. One of the reasons for this is probably the fact that the journal in which SHULGIN'S paper was published is just as inaccessible as the one in which BOROVSKY'S memoir appeared.

The only reference to SHULGIN'S observations which I have been able to discover is a statement occurring in LAVERAN'S monograph that " Shulgin croyait que les moustiques étaient les agents de transmission du bouton d'Orient " (LAVERAN, 1917, p. 437*).

It is not indicated, however, that this was actually the first suggestion of the rôle of blood-sucking insects in the transmission of this disease. On the contrary, the preceding paragraph—according to which " dès 1875, SÉRIZIAT déclarait avoir vu des boutons de Biskra ayant incontestablement pour origine des piqûres de moustiques " (*loc. cit.*, p. 437)—might be construed as establishing the priority of SÉRIZIAT, but from an extract of this author's writings appearing

*LAVERAN, A. (1917). *Leishmanioses*. (Paris : Masson et Cie.)

elsewhere in the monograph (*loc. cit.*, pp. 429-430) it is obvious that SÉRIZIAT merely asserted that the slightest lesion in the skin may serve as the starting point of oriental sore, and that he himself had seen sores originating at the site of a mosquito-bite. He did not, therefore, imply that the disease was disseminated by the mosquito, but that this insect was one of the agents, including mechanical ones, capable of impairing the intactness of the skin and thereby exposing it to infection.

SHULGIN's paper—" The question of the aetiology of Pendeh sore "—was written in Russian and published in the journal *Russkij Vrač* [= The Russian Physician], 1902, Nos. 32 and 33, pp. 1150 and 1180. These issues are unobtainable in this country, and I am indebted to the late Prof. G. W. EPSTEIN, of Moscow, for a typewritten *verbatim* copy of SHULGIN's article, from which I have translated the most interesting passages relating to the transmission of oriental sore.

After discussing the views of other Russian observers, who believed that the causative organism was found in water, or in the soil, and was disseminated by dust through the air, SHULGIN proceeds as follows :—

" However, I am inclined to consider that the mode of penetration of the infective agent into the body is the same as that recognized at present for marsh fever, *i.e.*, that it has an intermediate host—a mosquito or some other nocturnal biting insect."

The author then goes on to substantiate his contention :—

" In eight cases I succeeded in observing the very earliest phase of the disease, the primary papule, [at a period] when it was even impossible to identify it with certainty, but from which a typical Pendeh sore developed later. It then appeared in the form of a reddish, raised, compact spot, as large as a lentil. In the middle there was always a darker point, similar to that in the centre of a mosquito or flea bite. Intelligent persons in whom I observed such primary papules testified that they had actually been bitten in these places by something on a previous evening. . . . Moreover, on the assumption that the infection is spread by insects, it is easy to explain why the sore appears only during a certain period of the year. In all the localities where the disease is endemic cases are observed at the end of summer and at the beginning of autumn exclusively. . . . This can be fully accounted for on the basis of the mosquito theory, for mosquitos appear in large numbers in July. The time between their appearance and the occurrence of the first cases of the disease is taken up by the infection [of the insects], the development of the microorganism in them, its inoculation [to man], and the incubation period. In October the mosquitos disappear and no fresh cases occur while the old sores sometimes persist for 2 years. . . . "

SHULGIN also quotes the following observation in support of his views : In a certain locality of Turkestan the officers and men of the garrison shared the same barracks, but cases of oriental sore occurred among the privates exclusively. According to the author, this was due to the fact that only the officers slept under mosquito-nets and were, therefore, protected from the bites of the insects.

Lastly, SHULGIN notes that the sores appear most frequently on those parts of the body which are covered in the daytime, but may be exposed in the night (arms, legs).

In conclusion, the author makes the following statement : " As I said at the beginning, the insect transmitting the infection must be nocturnal, and now I more definitely attribute it to the mosquitos."

In the foregoing passages the case is presented in such a lucid manner and the arguments brought forward are so convincing that no special comments are required. It will be noted how near SHULGIN was to the correct solution of the nature of the vector of oriental sore, for all the observations and arguments adduced by him in support of his hypothesis regarding the transmission of the infection by mosquitos are equally applicable to the sandflies, which, in Turkestan, usually make their appearance in the middle of June and disappear towards the beginning of October, while the similarity of the feeding habits of both these groups of insects is well known.

Printed in Great Britain by H. R. GRUBB, LTD., Croydon.

H. R. GRUBB, LTD.,
PRINTERS,
POPLAR WALK, CROYDON.